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Primate skeletal epigenetics: evolutionary implications of DNA methylation patterns and their phenotypic association in primate skeletal tissues

Genevieve Housman
University of Chicago, USA

Introduction: Epigenetic signatures can be inherited and respond to environmental effects. Thus, it is difficult to determine whether epigenetic mechanisms that contribute to the expression of diverse phenotypes across species are the result of inheritance, environmental influences, or both. One way to better isolate these driving forces is by evaluating epigenetic patterns and their associated phenotypes both intra- and inter-specifically. Inter-specific studies have been initiated in primates, and some evolutionarily divergent DNA methylation patterns have been associated with phenotypes. However, this research is limited by the inclusion of only a couple species, and the effects of intra-specific variation on phenotypes have not been readily studied in nonhuman primates. The current study expands on this exploratory work by assessing the evolutionary relationship of DNA methylation in the skeletal tissues of several primate species and by examining how this variation relates to aspects of skeletal development and maintenance.

Methods: Methylation patterns were assessed in femoral bone and cartilage from five nonhuman primate species using Infinium MethylationEPIC arrays. Nonpathological femur morphologies were measured among species, and the degree of osteoarthritis, a disorder characterized by the breakdown of bone and cartilage, was also assessed within baboons.

Results: Several phylogenetically distinct methylation patterns are present, which may contribute to inter-specific morphological differences. However, intra-specific methylation and morphological variation are not related. Conversely, several intra-specific methylation changes are associated with osteoarthritis in baboons, and some patterns are conserved with those known in humans.

Conclusions: Overall, these findings reveal a range of evolutionarily conserved and divergent methylation patterns in the skeletal tissues of primates. Additionally, intra- and inter-specific methylation variation appears to differentially contribute to healthy and diseased skeletal phenotypes. This work informs our understanding of how epigenome evolution relates to skeletal phenotypes, and this research perspective may provide further insights into other healthy and disease phenotypes.